

WHAT IS CLAIMED IS:

✓ *Spa* 1. A gene delivery system for the genetic manipulation of immune system cells, comprising:

- 5 (a) an adenovirus; and  
(b) a component recognizing CD40 antigen.

*2* 2. The gene delivery system of claim 1, wherein said component recognizing CD40 antigen comprises:

- 10 a first antibody, or fragment thereof, directed against a fiber-knob protein of the adenovirus, and  
a second antibody, or fragment thereof, directed against CD40 antigen.

*Sub A2* 15 3. The gene delivery system of claim 2, wherein said first antibody and second antibody are genetically fused together.

4. The gene delivery system of claim 2, wherein said antibody directed against CD40 antigen is selected from the group  
20 consisting of G28.5 and FGK45.

5. The gene delivery system of claim 1, wherein said genetic manipulation is selected from the group consisting of transduction, immunomodulation and maturation.

5 6. The gene delivery system of claim 1, wherein said system further comprises a therapeutic gene.

7. The gene delivery system of claim 6, wherein said therapeutic gene is selected from the group consisting of a gene encoding a tumor antigen, a gene encoding an antigen for an infectious agent, a gene encoding an autoimmune antigen, an immunomodulatory gene and a gene encoding a cytotoxic agent.

8. The gene delivery system of claim 7, wherein said tumor antigen is human papillomavirus type 16 E7 antigen.

9. The gene delivery system of claim 1, wherein said immune system cells are selected from the group consisting of dendritic cells and B cells.

10. The gene delivery system of claim 9, wherein said dendritic cells are selected from the group consisting of monocyte-derived dendritic cells, bone marrow-derived dendritic cells and cutaneous dendritic cells.

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*Sueat* 11. A method for genetically manipulating immune system cells in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 1 to said individual.

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*Sueat* 12. The method of claim 11, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.

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13. The method of claim 11, wherein said administration of the gene delivery system is selected from the group consisting of systemic administration, intradermal administration and *ex vivo* administration.

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Sub 05 14. A method for genetically manipulating immune system cells in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 6 to said  
5 individual.

Sub 02 15. The method of claim 14, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection  
10 and an autoimmune disease.

16. The method of claim 14, wherein said administration of the gene delivery system is selected from the group consisting of systemic administration, intradermal  
15 administration and *ex vivo* administration.

Sub 06 17. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:  
20 administering the gene delivery system of claim 1 to said individual.

18. The ~~method~~ of claim 17, wherein said immunotherapy is vaccination.

5 ~~Sub 184~~ 19. The method of claim 17, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.

10 20. The method of claim 17, wherein said administration of the gene delivery system is selected from the group consisting of systemic administration, intradermal administration and *ex vivo* administration.

15 ~~Sub A7~~ 21. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 6 to said individual.

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22. The method of claim 21, wherein said immunotherapy is vaccination.

23. The method of claim 21, wherein said individual  
5 has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.

24. The method of claim 21, wherein said  
10 administration of the gene delivery system is selected from the group consisting of systemic administration, intradermal administration and *ex vivo* administration.

25. The gene delivery system of claim 1, wherein said  
15 system is a recombinant adenoviral vector.

26. The gene delivery system of claim 6, wherein said system is a recombinant adenoviral vector.

27. The method of claim 11, wherein said gene delivery  
20 system is a recombinant adenoviral vector.

28. The method of claim 14, wherein said gene delivery system is a recombinant adenoviral vector.

5            29. The method of claim 17, wherein said gene delivery system is a recombinant adenoviral vector.

30. The method of claim 21, wherein said gene delivery system is a recombinant adenoviral vector.

10            *Sub 28* 31. A recombinant adenoviral vector, comprising:  
a genetically modified adenovirus, wherein the modification targets said vector to CD40.

15            32. The recombinant adenoviral vector of claim 31, wherein the fiber of the adenovirus is replaced with two protein moieties, wherein first protein moiety initiates and maintains the trimeric configuration of the fiber protein, and wherein second protein moiety serves as a receptor-specific cell-binding ligand.

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33. The recombinant adenoviral vector of claim 32, wherein said first protein moiety is bacteriophage fibritin molecule, and wherein said second protein moiety is CD40 ligand.

5                    34. A gene delivery system for the genetic manipulation of immune system cells, comprising:

the recombinant adenoviral vector of claim 31.

10                    35. The gene delivery system of claim 34, wherein said genetic manipulation is selected from the group consisting of transduction, immunomodulation and maturation.

15                    36. The gene delivery system of claim 34, wherein said immune system cells are selected from the group consisting of dendritic cells and B cells.

20                    37. The gene delivery system of claim 36, wherein said dendritic cells are selected from the group consisting of monocyte-derived dendritic cells, bone marrow-derived dendritic cells and cutaneous dendritic cells.



38. The gene delivery system of claim 34, further comprising:

a tumor antigen expression cassette, wherein said cassette is inserted into the E1 region of the modified adenovirus.

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39. The gene delivery system of claim 38, wherein said tumor antigen is human papillomavirus type 16 E7 antigen.

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10 *Jul 10* 40. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 34 to said individual.

15 *Jul 08* 41. The method of claim 40, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.

20 42. The method of claim 40, wherein said administration of the gene delivery system is selected from the

group consisting of systemic administration, intradermal administration and *ex vivo* administration.

5 ~~43. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:~~  
~~administering the gene delivery system of claim 38 to said individual.~~

10 ~~44. The method of claim 43, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.~~

15 ~~45. The method of claim 43, wherein said administration of the gene delivery system is selected from the group consisting of systemic administration, intradermal administration and *ex vivo* administration.~~

Sub 2

46. The recombinant adenoviral vector of claim 31, wherein the fiber knob domain of the adenovirus is replaced with globular domain of CD40 ligand.

5            47. A gene delivery system for the genetic manipulation of immune system cells, comprising:  
the recombinant adenoviral vector of claim 46.

10           48. The gene delivery system of claim 47, wherein said genetic manipulation is selected from the group consisting of transduction, immunomodulation and maturation.

15           49. The gene delivery system of claim 47, wherein said immune system cells are selected from the group consisting of dendritic cells and B cells.

20           50. The gene delivery system of claim 49, wherein said dendritic cells are selected from the group consisting of monocyte-derived dendritic cells, bone marrow-derived dendritic cells and cutaneous dendritic cells.

51. The gene delivery system of claim 47, further comprising:

a tumor antigen expression cassette, wherein said cassette is inserted into the E1 region of the modified adenovirus.

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52. The gene delivery system of claim 51, wherein said tumor antigen is human papillomavirus type 16 E7 antigen.

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10 *Sub A13* 53. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 47 to said individual.

15 *Sub D10* 54. The method of claim 53, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection and an autoimmune disease.

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55. A method for enhancing dendritic cell-based immunotherapy in an individual in need of such treatment, comprising the step of:

administering the gene delivery system of claim 51 to  
5 said individual.

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56. The method of claim 55, wherein said individual has a disease selected from the group consisting of cancer, an infectious disease, allotransplant rejection, xenotransplant rejection  
10 and an autoimmune disease.

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